AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Previously presented) A compound of the formula I or II:

wherein

n is 1 or 2;

 R^{28} and R^{43} are independently selected from the group consisting of H and an aliphatic, acyl, aroyl or heteroaroyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^AR^B$, $-NR^BC(O)R^A$, $-NR^BC(O)OR^A$, $-NR^BSO_2R^A$, $-NR^BSO_2NR^AR^B$ or $-NR^BC(O)NR^AR^B$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:

where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety; where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety; where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; and

where each acyl moiety is an independently chosen -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

or a pharmaceutically acceptable salt thereof.

- 2. (Currently amended) The compound of claim 1, 78 or 79 wherein n is 2, \mathbb{R}^{28} is H, \mathbb{R}^{7a} is -OMe, \mathbb{R}^{7b} is H and \mathbb{R}^{43} is an aliphatic moiety.
- 3. (Currently amended) The compound of claim 1,78 or 79 wherein R^{7a} is -OMe and R^{7b} is H.

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- 4. (Currently amended) The compound of claim 1, 78 or 79 wherein R²⁸ is H.
- 5. (Currently amended) The compound of claim 1, 78 or 79 wherein R⁴³ is H.
- 6. (Currently amended) The compound of claim 1, 78 or 79 wherein either R^{7a} is a moiety other than -OMe or R^{7b} is a moiety other than H.
- 7. **(Previously Presented)** The compound of claim 6 wherein one of R^{7a} and R^{7b} is NR^BC(O)R^A, -NR^BC(O)OR^A, -NR^BSO₂R^A, -NR^BSO₂NR^AR^B or -NR^BC(O)NR^AR^B.
- 8. (Original) The compound of claim 7 in which R^B is H, OH or alkyl.
- 9. (Currently amended) The compound of claim 1, 78 or 79 wherein R⁴³ is an aliphatic moiety.
- 10. (Previously Presented) The compound of claim 9 wherein R⁴³ is an alkyl moiety.
- 11. (Currently amended) The compound of claim $\frac{10}{1,78}$ or $\frac{79}{2}$ wherein the alkyl moiety $\frac{R^{43}}{1}$ is a hydroxyalkyl moiety.
- 12. (Previously Presented) The compound of claim 9 wherein R⁴³ is an alkenyl moiety.
- 13. **(Previously Presented)** The compound of claim 12 wherein the alkenyl moiety is an allyl group.
- 14. (Currently amended) The compound of claim 1, 78 or 79 wherein R⁴³ is an acyl moiety.
- 15. (Canceled)
- 16. (Previously Presented) The compound of claim 14 wherein R⁴³ is an acyl moiety of the

formula R^AR^BN-alkyl-C(O)-.

17. (Original) The compound of claim 2, wherein R²⁸ and R⁴³ are H, R^{7a} is -OMe, and R^{7b} is H.

- 18. (Previously Presented) The compound of claim 6 wherein n is 2, and R²⁸ and R⁴³ are H.
- 19. (Currently amended) The compound of any of claims 1, 3-14, 16, 22, 23, 89 or 90 claim 1, 78 or 79 wherein n is 2.

20-21. (Canceled)

- 22. (Currently amended) The compound of claim 1, 78 or 79 wherein the compound has the formula II in which -OR⁴³ is in the S orientation.
- 23. (Currently amended) The compound of claim 1, $\underline{78 \text{ or } 79}$ wherein the compound has the formula II in which $-OR^{43}$ is in the R orientation.

24-40. (Canceled)

- 41. (Currently amended) A composition comprising a compound of any of claims 1-18, 22-23, 89 or 90 claim 1, 78 or 79 and one or more pharmaceutically acceptable carriers, diluents or excipients.
- 42. (Currently amended) A method for producing a compound of claim 1, 78 or 79 which comprises contacting a homologous C28 epimer with a titanium tetraalkoxide reagent under suitable conditions and for a sufficient time to permit epimerization.
- 43. (Original) The method of claim 42 wherein the titanium tetraalkoxide reagent is titanium tetraisopropoxide.

- 44. **(Previously Presented)** The method of claim 42 which further comprises recovering the epimerized product.
- 45. (Currently amended) The method of any of claims 42-44 claim 42 wherein the homologous C28 epimer is rapamycin.

46-77. (Canceled)

78. (Currently amended) The compound of any of claims 1-18, 22-23, 89 or 90 A compound of the formula I or II:

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wherein

n is 1 or 2;

R²⁸ and R⁴³ are independently selected from the group consisting of H and an aliphatic, acyl, aroyl or heteroaroyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, -R^A, -OR^A, -SR^A, -OC(O)R^A, -OC(O)NR^AR^B,
-NR^AR^B, -NR^BC(O)R^A, -NR^BC(O)OR^A, -NR^BSO₂R^A, -NR^BSO₂NR^AR^B' or -NR^BC(O)NR^AR^B'; or
R^{7a} and R^{7b} taken together, are H in the tetraene moiety:

where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

where each acyl moiety is an independently chosen -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each aliphatic, acyl, aroyl, heteroaroyl, heteroaliphatic, aryl or heteroaryl moiety contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties;

where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety; or a pharmaceutically acceptable salt thereof.

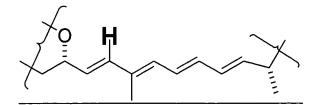
79. (Currently amended) The compound of any of claims 1-18, 22-23, 89 or 90 A compound of the formula I or II:

wherein

n is 1 or 2;

R²⁸ and R⁴³ are independently selected from the group consisting of H and an aliphatic, acyl, aroyl or heteroaroyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^AR^B$, $-NR^BC(O)R^A$, $-NR^BC(O)OR^A$, $-NR^BSO_2R^A$, $-NR^BSO_2NR^AR^B$ or $-NR^BC(O)NR^AR^B$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

where each acyl moiety is an independently chosen -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each aroyl, heteroaroyl, aryl or heteroaryl moiety contains one or more optional substituents selected from the group consisting of hydroxy, C1-C8 alkoxy, C1-C8 branched or straight-chain alkyl, acyloxy, carbamoyl, amino, N-acylamino, nitro, halo, trihalomethyl, cyano, and carboxyl;

or a pharmaceutically acceptable salt thereof.

80. (Currently amended) The compound of any of claims 10, 12 or 14 A compound of the formula I or II:

wherein

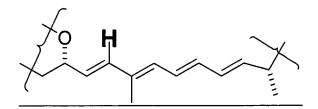
n is 1 or 2;

 R^{28} is selected from the group consisting of H and an aliphatic, acyl, aroyl or heteroaroyl moiety; R^{43} is an alkyl, alkenyl or acyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, -R^A, -OR^A, -SR^A, -OC(O)R^A, -OC(O)NR^AR^B,

-NR^AR^B, -NR^BC(O)R^A, -NR^BC(O)OR^A, -NR^BSO₂R^A, -NR^BSO₂NR^AR^B' or -NR^BC(O)NR^AR^B'; or

R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

where each acyl moiety is an independently chosen -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each alkyl, alkenyl or acyl moiety contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties; where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety; or a pharmaceutically acceptable salt thereof.

81. (Previously presented) 28-epirapamycin or a pharmaceutically acceptable salt thereof.

- 82. (Previously presented) 29-epirapamycin or a pharmaceutically acceptable salt thereof.
- 83. (**Previously presented**) 28, 29-bis-epirapamycin or a pharmaceutically acceptable salt thereof.
- 84. (Currently amended) The A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin of any of claims 81-83 in which except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, acyl, aroyl or heteroaroyl moiety; where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms; where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms; where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety; where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; and where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

or a pharmaceutically acceptable salt thereof.

85. (Currently amended) The compound of claim 84 A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, acyl, aroyl or heteroaroyl moiety; where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms; where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms; where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety; where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

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where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each aliphatic, acyl, aroyl or heteroaroyl moiety contains one or more optional substituents selected from the group consisting of -OH, -OR 2 , -SH, -SR 2 , -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH $_2$ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO $_2$ -CF $_3$, -OSO $_2$ F, -OS(O) $_2$ R 11 , -SO $_2$ -NHR 11 , -NHSO $_2$ -R 11 , sulfate, sulfonate, aryl and heteroaryl moieties; where R 2 is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and where R 11 is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety; or a pharmaceutically acceptable salt thereof.

86. (Currently amended) The compound of claim 84 A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR 43 wherein R 43 is an aliphatic, acyl, aroyl or heteroaroyl moiety; where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms; where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms; where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety; where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each aroyl or heteroaroyl moiety contains one or more optional substituents selected from the group consisting of hydroxy, C1-C8 alkoxy, C1-C8 branched or straight-chain alkyl, acyloxy, carbamoyl, amino, N-acylamino, nitro, halo, trihalomethyl, cyano, and carboxyl; or a pharmaceutically acceptable salt thereof.

87. (Currently amended) The compound of claim 84 A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, acyl, aroyl or heteroaroyl moiety;

where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms; where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms; where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety; where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein R^{43} is a hydroxyalkyl moiety that contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties; where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety; or a pharmaceutically acceptable salt thereof.

88. (Currently amended) The compound of claim 84 A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, acyl, aroyl or heteroaroyl moiety; where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms; where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms; where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety; where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

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wherein R⁴³ is an acyl moiety that contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties; where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety; or a pharmaceutically acceptable salt thereof.

- 89. (Currently amended) The compound of claim 1, 78 or 79, wherein the compound has the formula I.
- 90. (Currently amended) The compound of claim 1, 78 or 79, wherein the compound has the formula II.